

CLAIMS

1. A method of producing an animal embryo, the method comprising transferring from a nuclear donor cell which has been selected on the basis that it is histone hypomethylated at least a portion of the nuclear contents including at least the minimum
5 chromosomal material able to support development into a suitable recipient cell.
2. The method of claim 1 wherein the nuclear donor cell has been selected by experimentally determining that a first cell is histone hypomethylated and selecting a second cell which is similar or identical to the first cell to thereby select a histone hypomethylated cell to be used as said nuclear donor cell.
- 10 3. The method of claim 2 wherein said first cell and second cell are from the same population of cells.
4. The method of claim 1 wherein the nuclear donor cell has been selected by selecting a cell of a type which has been previously determined as being histone hypomethylated or which has been previously determined as being likely to be histone
15 hypomethylated.
5. The method of any one of claims 2 to 4 wherein the level of histone methylation of said first cell or of said cell type when histone hypomethylated is negligible or absent.
6. The method of any one of claims 2 to 5 wherein the level of histone methylation of said first cell or of said cell type when histone hypomethylated is assessed on the basis of
20 methylation at one or more residues of H3.
7. The method of any one of claims 2 to 6 wherein the level of histone methylation of said first cell or of said cell type when histone hypomethylated is assessed on the basis of methylation at one or more lysine residues.
8. The method according to claim 7 wherein the level of histone methylation is
25 assessed on the basis of methylation at one, two, three or four of the following lysine residues: residues H3^{K4}, H3^{K9}, H3^{K27} and H3^{K36}.
9. The method according to claim 8 wherein the level of histone methylation is assessed on the basis of methylation at H3^{K4} and H3^{K9}.
10. The method according to any one of the preceding claims wherein the nuclear
30 donor cell is a mammalian cell.

11. The method according to any one of the preceding claims wherein the recipient cell is a mammalian cell.
12. The method according to any one of the preceding claims wherein the recipient cell is an enucleated oocyte.
- 5 13. A method of producing an animal embryo, the method comprising transferring from a nuclear donor cell at least a portion of the nuclear contents including at least the minimum chromosomal material able to support development into a suitable recipient cell wherein the nuclear donor cell is obtained from an embryo obtained by the method of any one of claims 1 to 12.
- 10 14. The method according to claim 13 wherein the nuclear donor cell has been selected on the basis that it is histone hypomethylated.
15. A method of producing a foetus, the method comprising allowing an embryo obtained by a method according to any one of claims 1 to 14 to develop into a foetus.
16. A method of producing a non-human animal the method comprising allowing an
15 embryo obtained by a method according to any one of claims 1 to 14 or a foetus obtained by a method according to claim 15 to develop into said non-human animal.
17. A method of producing an embryonic stem cell line, the method comprising transferring an embryo obtained by the method of any one of claims 1 to 14 to a culture system.
- 20 18. A method of producing an embryonic stem cell line, the method comprising isolating the inner cell mass of an embryo obtained by the method of any one of claims 1 to 14 and transferring the inner cell mass to a culture system.
19. A method according to any one of the preceding claims wherein the nuclear donor cell is a non-human cell.
- 25 20. A method according to any one of the preceding claims wherein the recipient cell is a non-human cell.
21. An embryo obtained by the method of any one of claims 1 to 14 wherein the embryo is preferably a non-human embryo.
22. A foetus obtained by the method of claim 15, wherein the embryo is preferably a
30 non-human foetus.

23. A non-human animal obtained by the method of claim 16.
24. An embryonic cell obtained by the method of claim 17 or 18, wherein the embryonic cell is preferably a non-human cell.
25. The use of histone hypomethylation status or histone methyl transferase expression
5 or activity as an indicator of the suitability of a cell to act as a nuclear donor cell.
26. A method of selecting a cell to be used as a nuclear donor cell, the method comprising selecting said cell on the basis that it is histone hypomethylated and optionally also on the basis that it has reduced expression or activity of a histone methyl transferase.
27. The use of a resting B or T lymphocyte or Kupfer cell as a nuclear donor cell.
- 10 28. The use of claim 27 wherein the resting B lymphocyte is a small resting B lymphocyte.
29. The use of claim 27 wherein the resting T lymphocyte is a small resting T lymphocyte.
30. The use of claim 28 wherein the small resting B lymphocyte is obtained by a
15 method comprising selecting a small B lymphocyte from a population of cells enriched for resting B lymphocytes.
31. The use of claim 29 wherein the small resting T lymphocyte is obtained by a method comprising selecting a small T lymphocyte from a population of cells enriched for resting T lymphocytes.
- 20 32. The use of claim 30 or 31 wherein one or more of the cells in the population of cells enriched for resting B lymphocytes or T lymphocytes are tested for histone hypomethylation.
33. The use of any one of claims 30 to 32 wherein one or more of the cells in the population of cells enriched for resting B or T lymphocytes are tested for reduced
25 expression or activity of a histone methyl transferase.